Remarks

Claims 156, 163, 175, 179-186, 190-192, 196-203, and 207-209 are now pending. Claims 1-155, 157-162, 164-174, 176-178, 187-189, 193-195, 204-206, and 210-241 are cancelled and claims 156, 163, 175, 179, 186, 190, 192, 196, 203, 207, and 209 are amended without prejudice or disclaimer of any previously claimed subject matter. Applicant has amended the claims to focus the present prosecution to compound and pharmaceutical composition claims wherein the 3'-moiety is an amino acid ester, i.e. $-OR^2$, wherein R^2 is an amino acid residue. Applicant reserves the right to prosecute the cancelled subject matter, including the compounds and pharmaceutical compositions wherein R^2 can be selected from the group consisting of straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, mono, di, or triphosphate, or a phosphate prodrug, in a continuation application.

Supplemental Information Disclosure Statement

Pursuant to the duty of disclosure under 37 CFR §§ 1.56, 1.97 and 1.98, Applicants cite the publications listed on the accompanying PTO-1449. Copies of all listed references are enclosed. The citation of this information does not constitute an admission of priority or that any cited item is available as a reference, or a waiver of any right the Applicant may have under the applicable statues, regulations and Rules of Practice in patent cases, or otherwise. Applicant respectfully request the Examiner acknowledge entry and consideration of the present Supplemental Information Disclosure Statement and Form 1449 submitted with this response.

Rejections under 35 U.S.C. § 102

Original claims 175-178, 181, 186-189, 192-195, 198, and 203-206 were rejected under 35 U.S.C. §102, allegedly because they are anticipated by U.S. Patent No. 5,559,101 to WEIS et

al., which teaches numerous α and β-L-ribofuranosyl nucleosides. Applicant respectfully disagrees. WEIS provides only a generic disclosure of numerous α and β-L-ribofuranosyl nucleosides, in that no 2'-deoxy-3'-O-substituted nucleosides are specifically named, but merely fall generically within the broad scope of the presented chemical formula. WEIS does not specifically disclose any β-L-2'-deoxy-3'-O-substituted-cytidines. In fact, WEIS actually teaches away from the β-L-2'-deoxy-3'-O-substituted-cytidines, because it clearly considers 3'-O-substitution only when the 5'-position also is substituted. Applicant has surprisingly discovered that β-L-2'-deoxy-3'-O-substituted-cytidines are particularly effective as prodrugs of β-L-2'-deoxy-cytidine, and thereby exhibits higher oral bioavailability than the parent with substantial activity against HBV.

However, to facilitate prosecution of the present case, Applicant has cancelled the embodiments directed to 3'-O-alkyl, 3'-O-aryl, 3'-O-arylsulfonyl, and 3'-O-aralkylsulfonyl prodrugs. Therefore, WEIS does not disclose or render obvious the claims as now presented, which are limited to compounds and pharmaceutical compositions wherein the 3'-moiety is an amino acid ester, i.e. $-OR^2$, wherein R^2 is an amino acid residue.

Original claims 175, 181, 186, 189, 192, 198, and 203 were rejected under 35 U.S.C. §102, allegedly because they are anticipated by U.S. Patent No. 5,416,203 (the '203 patent) to LETSINGER, which teaches oligonucleotides compounds conjugated to a steroid via the 3'-phosphate. Applicant respectfully disagrees. In order to constitute anticipation, each and every element of the claim must be disclosed by the prior art reference. The claimed invention differs from the LETSINGER reference in that the claims of the present invention are not directed to oligonucleotides, rather they are directed to β-L-2'-deoxy-3'-O-substituted-cytidine. Since the reference fails to teach nucleosides, and in particular β-L-2'-deoxy-3'-O-substituted-cytidines, it cannot anticipate the claimed invention. Likewise, LETSINGER cannot render the present claims obvious under 35 USC 103. One of ordinary skill in the art would not have been motivated to remove a cytidine nucleoside from the disclosed oligonucleotide chain to obtain a 3'-prodrug as presently claimed.

However, to facilitate prosecution of the present case, Applicant has cancelled the embodiments directed to 3'-O-phosphate prodrugs. Therefore, LETSINGER does not disclose the claims as now presented, which are limited to compounds and pharmaceutical compositions wherein the 3'-moiety is an amino acid ester, i.e. $-OR^2$, wherein R^2 is an amino acid residue.

The Examiner has acknowledged that claims 156, 163, 179, 180, 182-185, 190, 191, 196, 197, 199-202, and 207-209 are directed to allowable subject matter as cytidine compounds that are 3'-O-substituted with an amino acid are an unobvious modification of the prior art of record. In view of the present amendment to limit the claims to cytidine compounds that are 3'-O-substituted with an amino acid and response to Office Action, Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Applicant does not believe any fee is due with this Amendment and Response to Office Action and Transmittal of Supplemental Information Disclosure Statement; however, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account 11-0980.

Respectfully submitted,

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Date: October 31, 2003

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